Medical Hypotheses 125 (2019) 89

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Long term drug related remission may encourage drug withdrawal in patients with rheumatoid arthritis

ARTICLE INFO

Keywords:
Drug free remission
Rheumatoid arthritis

ABSTRACT

Remission is the goal of therapy in patients with rheumatoid arthritis (RA). However, drug free remission has not been investigated adequately. Early and intensive treatment may increase the chances of successful drug free remission. Effect of long term remission while on medical therapy on the success of drug withdrawal has not been previously evaluated in RA. Long term immune suppression has been shown to have beneficial effects on relapse rates in other diseases with dysregulated immune tolerance. Therefore, drug withdrawal could be an acceptable option in RA patients in long term remission.

Dear Editor,

Rheumatoid arthritis (RA) is a multi-systemic auto-immune disease with mainly chronic inflammatory joint involvement. Loss of immune tolerance due to genetic and environmental factors may be among the main irregularities in the pathogenesis. Recently, sustained drug free remission has become one of the eventual treatment targets for RA. Unfortunately, observational cohort studies conducted in the last two decades reported that only 10–15% of the RA patients have achieved sustained drug free remission [1]. Early and intensive treatment strategies with new treatment options were found to be the foremost factors related to sustained drug free remission in RA [2]. Furthermore, it has been hypothesized that treatment during windows of opportunity period could re-establish immune tolerance and help to achieve sustained drug free remission goal [3]. Moreover, long term successful immune modulation or immune suppression has been associated with drug free survival in solid organ transplantation [4–6] or drug free remission in graves' disease [7]. Tamai et al. have investigated the relationship between duration of therapy and relapse rate in Graves' disease [7]. By the end of the first year of drug-free period, relapse rate was 69% with six month treatment, while 18% with 24 month treatment [7]. Likewise, duration of therapy has played significant role in successful immunosuppressive withdrawal after liver transplantation. Herein, 13% of the patients on therapy for six years and 79% of those on therapy for 11 years successfully withdrew their immunosuppressant [5]. In these cases, long term suppression of immune system may activate regulatory pathways and establish stable cellular regulation [8]. These findings may be applicable for RA. In fact, major studies conducted in RA cohorts found significant associations between early and intensive treatment strategies with higher rates of drug free remission. However, neither these studies, nor other observational or cross sectional studies evaluated the relationship between the duration of remission while on medical therapy and successful drug withdrawal in patients with early or established RA. In patients with other diseases with dysregulated immune tolerance, long term drug related remissions have reduced drug free relapse rates [9]. Therefore, we can hypothesize that, total or partial drug withdrawal could be conceivable in RA patients under long term remission.

Acknowledgement

None.

Conflict of interest

I have declared no conflict of interest.

Funding

None.

References

[1] Ajeganova S, Huizinga T. Sustained remission in rheumatoid arthritis: latest evidence and clinical considerations. Therapeut Adv Musculoskel Dis 2017;9:249–62.
[2] Nagy G, van Vollenhoven RF. Sustained biologic-free and drug-free remission in rheumatoid arthritis, where are we now? Arthritis Res Therap 2015;17:181.
[3] Boers M. Understanding the window of opportunity concept in early rheumatoid arthritis. Arthrit Rheumat 2003;48:1771–4.
[4] Wekerle T. Immune tolerance in transplantation. Clin Exp Immunol 2017;189:133–4.
[5] Adams DH, Sanchez-Fueyo A, Samuel D. From immunosuppression to tolerance. J Hepatol 2015;62:S170–85.
[6] Casiraghi F, Cortinovis M, Perico N, Remuzzi G. Recent advances in immunosuppression and acquired immune tolerance in renal transplants. Am J Physiol Ren Physiol 2016;310:F446–53.
[7] H. Tamai T. Nakagawa O. Fukino et al. Thionamide therapy in Graves' disease: relation of relapse rate to duration of therapy Ann Int Med 92 1980 488 490.
[8] Nepom GT, St Clair EW, Turka LA. Challenges in the pursuit of immune tolerance. Immunol Rev 2011;241:49–62.
[9] van Nies JA, Krabben A, Schoones JW, Huizinga TW, Kloppenburg M, van der AH. Helm-van Mil, What is the evidence for the presence of a therapeutic window of opportunity in rheumatoid arthritis? A systematic literature review. Ann Rheum Dis 2014;73:861–70.

Mehmet Engin Tezcan[1]
M.D., Kartal Dr. Lutfi Kirdar Training and Research Hospital, Department of Rheumatology, Kartal, 34680 Istanbul, Turkey
E-mail address: kartalromatoloji@gmail.com.

[1] Orcid ID: 0000-0002-1753-4936.

https://doi.org/10.1016/j.mehy.2019.02.038
Received 22 December 2018; Accepted 15 February 2019